UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/383,551	08/26/1999	TAKUYA TAMATANI	06501/039001	6738

7590 01/17/2002

JANIS K FRASER PH D J D
FISH & RICHARDSON PC
225 FRANKLIN STREET
BOSTON, MA 021102804

EXAMINER
ROARK, JESSICA H

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 01/17/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/383,551	Applicant(s) TAMATANI ET AL.	
	Examiner Jessica H. Roark	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/26/99, 2/15/01, 5/17/01, 6/25/01 and 11/9/01*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) *1-26,35 and 36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5,17,23* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's amendments to the specification, filed 10/26/99, 2/15/01, 5/17/01, 6/25/01 and 11/9/01 (Paper Nos. 6, 11, 15, 18 and 22), are acknowledged.

Claims 1-36 *are pending.*

2. Applicant's election without traverse of Group III (claims 27-34) in Paper No. 21 is acknowledged.

Claims 1-26 and 35-36 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

Claims 27-34 *are under consideration in the instant application.*

3. Sequence compliance: The instant application appears to be in sequence compliance for patent applications containing nucleotide sequence and/or amino acid sequence disclosures.

4. Priority: Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

However, English translations for foreign priority documents JP 9/62290 and JP 10/62217, as well as for PCT/JP98/00837, of which USSN 09/383,551 is a CIP; have not been provided. Although certain aspects of the instantly recited claims do appear to be supported in the foreign priority documents and PCT/JP98/00837, it is unclear whether the foreign priority documents or PCT/JP98/00837 provide adequate written description for the instant claims.

Therefore, certain rejections set forth herein *do not rely upon either Applicant's foreign priority date or the filing date of PCT/JP98/0083, in the absence of certified translations* of said documents and the absence of a clear record that there is written support for the instant claims.

Applicant is reminded that such priority for the instant limitations requires written description and enablement under 35 U.S.C. 112, first paragraph.

5. Applicant's IDSs, filed 1/4/00, 5/23/01 and 12/31/01 (Paper Nos. 5, 17 and 23), are acknowledged.

6. The abstract and title of the invention are not descriptive. A new abstract and title are required that are clearly indicative of the invention *to which the claims are directed.*

In addition, Applicant should avoid the use of novel in the abstract, as patents are presumed to be novel and unobvious.

7. Formal drawings have been submitted which fail to comply with 37 CFR 1.84.
Please see the enclosed form PTO-948.

8. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

In particular, Applicant is requested to review the application for embedded hyperlinks and/or other forms of browser-executable code and delete them. Embedded hyperlinks and/or other form of browser-executable code are impermissible in the text of the application as they represent an improper incorporation by reference. See MPEP § 608.01 and 608.01(p).

Hyperlinks have been noted at least on page 34 at line 20.

9. Claims 27-34 are objected to under 37CFR 1.821(d) because claim 1, from which each of these claims depends either directly or indirectly, fails to recite the SEQ ID NOS for the sequences recited in sections (d) and (e).

10. Claims 30-31 are objected to for the following informality: in view of the dependency of each of these claims upon (non-elected) claim 1, the recitation of "or the cell surface molecule comprising said polypeptide" is redundant since claim 1 requires in the preamble that the polypeptide be a cell surface molecule. It is suggested that Applicant delete the redundant language.

11. Claim 29 is objected to for the following informality: in view of the dependency of claim 29 upon (non-elected) claim 14, the recitation of "or the human-derived cell surface molecule comprising said polypeptide" is redundant since claim 14 requires that the polypeptide be a human-derived cell surface molecule. It is suggested that Applicant delete the redundant language.

12. 35 U.S.C. § 101 reads as follows:

> *"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".*

13. Claim 27 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter; a product of nature.

The polypeptide as claimed has the same characteristics and utility as the polypeptide found naturally expressed on cellular surfaces; therefore it does not constitute statutory subject manner. In the absence of the hand of man, the naturally occurring polypeptide is considered non-statutory subject matter. Diamond v. Chakrabarty, 206 U.S.P.Q. 193 (1980).

It is suggested that Applicant indicate that the "antibody" is isolated and/or purified.

14. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 27-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 27-34 are indefinite in that they are dependent on non-elected claims. The claims should be re-written such that the limitations of the non-elected claims are recited and the elected claims no longer depend upon non-elected claims.

B) Claims 27-34 are indefinite in the recitation (via direct or indirect dependence from non-elected claim 1) of "*constituting*". The term "*constituting*" is not defined by the claim, nor does it appear to be defined in the specification. One of ordinary skill in the art would not be reasonably apprised of the metes and bounds of this term. For example, is "constituting" considered open (i.e.,. "comprising") or closed (i.e., "consisting of") language, or is it intended to indicate properties of the polypeptide?

It is suggested that the claim be amended to recite simplified claim language consistent with US practice, taking into account the rejections set forth herein.

C) Claim 27 is indefinite and ambiguous in that the claim language appears to encompass in the alternate an antibody or a cell surface molecule comprising the polypeptide of claim 1. The language is also confusing since claim 1 (from which claim 27 depends) requires in its preamble that the polypeptide is a cell surface molecule.

It is suggested that Applicant simplify the claim language by eliminating the redundant phrase ", or the cell surface molecule comprising said polypeptide".

D) Claims 29 and dependent claims 32-33 recite the limitation "human-derived". However, this language is ambiguous in that it is unclear if "derived" means that the polypeptide is of human origin (i.e., isolated from a human), or if the term "derived" means that the polypeptide is a human polypeptide that has been mutated, or possibly a polypeptide produced from DNA isolated from any species but expressed in a human host cell.

E) The term "substantially" in claims 30 and 31is a relative term which renders the claim indefinite. The term "substantially" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention.

It is suggested that Applicant delete "substantially".

F) The phrase "substantially the same as the effect of..." in claims 30 and 31is ambiguous. Since no particular testable "effect(s)" is recited, one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention. In addition, it is unclear if the recited antibody must have all the same "effects" as the references antibodies, or only one shared "effect".

It is suggested that Applicant delete "substantially" and provide claim language *which sets forth testable* "effects" of the reference antibodies, as supported by the specification as filed.

G) Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

16. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

17. Claims 27-34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The following *written description* rejection is set forth herein.

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 3rd column).

There does not appear to be an adequate written description in the specification as-filed for the genus of antibodies to a genus of polypeptides comprising "a cell surface molecule (a) expressed at least in thymocytes and mitogen-stimulated lymphoblasts; (b) an antibody to which induces cell adhesion between mitogen-stimulated lymphoblasts; (c) an antibody to which induces proliferation of peripheral blood lymphocytes in the presence of an antibody to CD3, (d) has a partial sequence FDPPPF in its extracellular region; and (e) has a partial amino acid sequence of YMFM in its cytoplasmic region" as recited via the dependency of the instant claims either directly or indirectly from non-elected claim 1. Applicant does not appear to have provided an essential structural feature that provides these recited functions of the polypeptide for which the antibody is specific. Nor does Applicant appear to have provided either an essential structure or function for antibodies recognizing the polypeptide genus.

The claims are drawn to antibodies recognizing a large genus of polypeptides. Although Applicant has isolated three naturally occurring polypeptides having the FDPPPF and YMFM motifs (from human, rat and mouse); Applicant does not appear to have demonstrated that these peptide motifs provide any of the recited or disclosed functions of the polypeptide recognized by the antibody. Nor does there appear to be any other functional characteristic shown to be coupled with these two polypeptide motifs, either singularly or in combination. In addition, although the specification discloses antibodies to the human polypeptide of SEQ ID NO:2, as well as to the rat polypeptide of SEQ ID NO:13; there does not appear to be a disclosed correlation between the structure of the antibodies and their general function of recognizing the broader genus of polypeptides having the recited characteristics.

Consequently, there does not appear to be an adequate written description of the genus of antibodies recognizing the polypeptides encompassed by the instant claim language.

Similarly, a nexus between a structure and function is also lacking for a "portion thereof" as recited in instant claims 28 and 32. While the specification does support a portion of an antibody that is reactive to the polypeptide (e.g., claim 29); the recitation as presented in claims 28 and 32 reads on *any portion of the portion* that is reactive with the polypeptide. These *subfragments* do not necessarily possess reactivity for the polypeptide and thus lack a correlation between structure and function. It is suggested that Applicant amend claims 28 and 32 to read "the antibody or portion thereof of claim...".

In addition, as noted supra, "derived" is an ambiguous term that encompasses sequences with unlimited mutations. Therefore, there does not appear to be an adequate written description of antibodies to "derived" polypeptides since the structure of such polypeptides is not defined.

There also does not appear to be an adequate written description in the specification as-filed for the genus of polypeptides comprising "an extracellular region" (as found in the language of claim 29, which depends from claim 14, which depends in turn from claim 13). Limiting the claims to "an extracellular region" does not correct the written description deficiencies noted supra. In addition, "an extracellular region" reads on subsequences, as disclosed in the specification on page 39 at lines 16-25. Applicant has reduced to practice two species of polypeptide fragments – that of the whole extracellular region of the rat polypeptide (e.g., residues 1-141 of SEQ ID NO:13) and the whole extracellular region of the human polypeptide (e.g., residues 1-141 of SEQ ID NO:2) and used these fragments to produce fusion proteins comprising an immunoglobulin hinge, C2 and C3 domains (Example 16 at pages 105-107). However, Applicant does not appear to have established which *subsequences* of the whole extracellular region of the rat or human polypeptide are essential for its function. Consequently, antibodies to these subsequences lack adequate written description.

Finally, while instant claims 30 and 31 recite that the genus of antibodies to the genus of polypeptides have "substantially the same effect" as two deposited antibodies, the instant claims do not recite testable functional properties (e.g., induce agglutination of rat thymocytes). In the absence of a defined structure, some functional characteristic must be shared by the genus of antibodies recited.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant is invited to point to clear support or specific examples of the claimed invention in the specification as-filed.

18. Claims 27-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for antibodies which react with polypeptides comprising SEQ ID NO:2, SEQ ID NO:13 or SEQ ID NO:14 or the whole extracellular domains thereof; does not reasonably provide enablement for an antibody to *any* polypeptide comprising "a cell surface molecule (a) expressed at least in thymocytes and mitogen-stimulated lymphoblasts; (b) an antibody to which induces cell adhesion between mitogen-stimulated lymphoblasts; (c) an antibody to which induces proliferation of peripheral blood lymphocytes in the presence of an antibody to CD3, (d) has a partial sequence FDPPPF in its extracellular region; and (e) has a partial amino acid sequence of YMFM in its cytoplasmic region", nor to various undefined subsequences or variants of the genus of polypeptides or to undefined subsequences of individual SEQ ID NOS. Likewise, the specification, while being enabling for the portion of an antibody that binds the polypeptide, does not reasonably provide enablement for *any* "portion thereof" of the antibody. In addition, although the specification is enabling for the monoclonal antibodies identified by Accession Nos. FERM BP-5707 and FERM BP-5708, it does not appear to be enabling for any antibody that has "substantially the same effect" as these antibodies. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Antibodies to the polypeptide genus:
SEQ ID NO:2, SEQ ID NO:13 and SEQ ID NO:14 are disclosed to each share in their extracellular region the sequence FDPPPF and in their intracellular region the sequence YMFM (e.g., Figure 10). However, the specification does not disclose and the state of the art does not appear to recognize that there is a nexus between these partial amino acid sequences and the function(s) of the polypeptide.

The specification discloses that the FDPPPF motif is important for binding an unidentified ligand (e.g., page 13 at lines 16-18) and that the YMFM motif is important for signal transduction (e.g., page 13 at lines 19-21). However, there does not appear to be data to support this disclosure other than a discussion that the FDPPPF and YMFM motifs are homologous to domains with these functions found in the costimulatory molecules CD28 and CTLA4 (e.g., Figures 11 and 12).

However, the skilled artisan would not reasonably expect that the FDPPPF sequence would be sufficient to confer the recited functional activities on a polypeptide expressing it in the absence of many other essential sequence-based structural constraints. Even in combination with the intracellular YMFM sequence, the skilled artisan would still require extensive guidance as to the nature of the sequence and structure of a polypeptide comprising these sequence motifs before the skilled artisan would have a reasonable expectation that the polypeptide comprising these motifs would have the recited expression and functional properties. For example, Bajorath (J. Mol. Modeling 1999; 5:169-176, see entire document) reviews that it was well known that the homologous MYPPPY motif in CD28 and CD152 (the "CD" designation of CTLA4) was only a part of the ligand binding site and that a variety of other residues were essential for ligand binding (see especially page 170, 2nd column).

Similarly, the term "derived" permits any number of substitutions, deletions or additions to a reference sequence; and thus does not provide sufficient guidance such that one skilled in the art could make and use the "derived" polypeptide without undue experimentation to determine which sequence were essential. Nor would the skilled artisan be able to make and use various undefined subsequences of the polypeptides, such as subsequences of the extracellular region, without undue experimentation to identify which sequence lengths were essential for any particular polypeptide function.

Thus in the absence of an enabling description of the genus of polypeptides, it would require undue experimentation of the skilled artisan to make and use antibodies to these polypeptides.

"Portions thereof" of the antibody
Neither would the skilled artisan recognize that *any* "portion thereof" of an antibody, as recited in instant claims 28 and 32, could be used to react to the polypeptide. Methods of making fragments involving the antigen binding domains were well known to the skilled artisan at the time the invention was made. However, the skilled artisan would not reasonably expect that *any* "portion thereof" of an antibody would bind antigen. For example, it was well known in the art at the time the invention was made that the portion of the antibody that is the Fc region would not bind the polypeptide antigen of interest. As noted supra, Applicant should amend claims 28 and 32 to read "antibody or portion thereof of claim...".

"Substantially the same as the effect of ..."
Finally, although the specification discloses functional properties of the deposited antibodies FERM BP-5707 and FERM BP-5708 on mitogen stimulate rat lymphoblast cells; as noted supra the phrase "substantially the same as the effect of..." is ambiguous and does not establish the metes and bounds of the invention. Given the ambiguity of the instant claim language, it would require undue experimentation of one skilled in the art to determine if a particular antibody has "substantially the same effect" as the reference antibodies. For example, since no particular testable "effect" is recited, the skilled artisan would be forced to evaluate the test antibody for every conceivable "effect", and such extensive experimentation of the skilled artisan is undue.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Without sufficient guidance as to the identity of the polypeptide against which the antibody is reactive, the portions of the antibody encompassed by instant claims, and the requisite function(s) ("effects") of the antibody; the experimentation left to one skilled in the art is unnecessarily, and improperly, extensive and undue.

19. In claims 30 and 31, it is apparent that the hybridomas FERM BP-5707 and FERM BP-5708 are required to practice the claimed invention. As required elements, they must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If they are not so obtainable or available, the enablement requirements of 35 U.S.C. 112, first paragraph, may be satisfied by a deposit of the pertinent hybridomas which produce these antibodies. See 37 CFR 1.801-1.809.

It is noted that page 78 of the specification at lines 18-25 indicates that these cell lines were deposited with the international depository authority the National Institute of Bioscience and Human-Technology on October 11, 1996 under the terms of the Budapest Treaty. In addition, Applicant has assured in Paper No. 22 (filed 11/9/01) that all restrictions will be irrevocably removed upon granting of a patent.

Therefore, the enablement requirement under 35 USC 112, first paragraph is considered to be fulfilled with respect to FERM BP-5707 and FERM BP-5708.

20. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

21. Claims 27-34 are rejected under 35 U.S.C. 102(a) as being anticipated by Hutloff et al. (Nature January 1999, 397:263-266, see entire document).

Hutloff et al. teach a monoclonal antibody (F44) to the human ICOS polypeptide (see entire document, e.g., page 263, 1st column).

Hutloff et al. teach that the anti-ICOS F44 antibody is a monoclonal antibody produced by an isolated hybridoma (e.g., page 266, last paragraph of Methods under "Cell preparation , T-cell activation and generation of monoclonal antibodies").

Hutloff et al. also teach a pharmaceutical composition comprising the F44 monoclonal antibody and a pharmaceutically acceptable carrier, since the F44 antibody was provided to cells in cell culture (see especially the legend to Figure 2).

Human ICOS is taught to be a polypeptide:

constituting a cell surface molecule (e.g., see Abstract or Figure 1a);

an antibody to which induces proliferation of peripheral blood lymphocytes in the presence of an antibody to CD3 (e.g., Figure 2);

has a partial amino acid sequence of FDPPPF in its extracellular region (e.g., Fig 1d); and

has a partial amino acid sequence of YMFM in its cytoplasmic region (e.g., Fig 1d).

The human ICOS sequence shown in Figure 1d is identical to instant SEQ ID NO:2. The Hutloff et al. polypeptide shown in Figure 2 comprises an extracellular region, and is derived (isolated) from a human.

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations, including that the antibody to the polypeptide induces adhesion between mitogen-stimulated lymphoblast cell would all be inherent properties of the F44 antibody and the polypeptide recognized by it. In addition, especially given the ambiguity noted supra with respect to instant claims 30 and 31; the F44 antibody would also inherently have an effect that is "substantially the same as the effect of" monoclonal antibodies FERM BP-5707 and FERM BP-5708. Finally, the intended use of the pharmaceutical composition comprising the antibody does not carry patentable weight per se, and the claims read on the active or essential ingredient of the composition.

As noted supra in the discussion of the priority date of the instant application, a showing that the instant claims have adequate support under 35 USC 112 first paragraph in PCT/JP98/00837 could be used to establish that Hutloff et al. is not available as prior art under 35 USC 102(a).

22. Claims 27-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Redoglia et al. (Eur. J. Immunol. November 1996; 26:2781-2789, IDS #AD, see entire document), as evidenced by Buonfiglio et al. (Eur. J. Immunol. December 2000; 30:3463-3467, IDS #AC) and as evidenced by Mages et al. (Eur. J. Immunol. April 2000; 30:1040-1047).

Redoglia et al. teach a monoclonal antibody (C398.4A) to the mouse polypeptide H4 (see entire document, e.g., Abstract).

Redoglia et al. teach that C398.4A is a monoclonal antibody produced by an isolated hybridoma (e.g., page 2782, section 2.1).

Redoglia et al. also teach a pharmaceutical composition comprising the C398.4A antibody and a pharmaceutically acceptable carrier since the C398.4A was provided to cells in cell culture (see especially the legends to Figures 1 and 2).

Mouse H4 is taught to be a polypeptide:
constituting a T cell surface molecule (e.g., see Abstract or Figure 3);
expressed at least on thymocytes and mitogen-stimulated lymphoblast cells (e.g., Figures 3 and 4);
and an antibody to which induces proliferation of peripheral lymphocytes in the presence of an antibody to CD3 (e.g., Figure 2 and related discussion).

Although Redoglia et al. do not test proliferation of peripheral *blood* lymphocytes (PBL), antibodies to H4 would also inherently stimulate PBL proliferation, especially given that antibodies to H4 stimulate proliferation of peripheral lymphocytes isolated from the spleen. In addition, the H4 polypeptide of Redoglia et al. is inherently a polypeptide fragment that comprises the extracellular region, given that the polypeptide can be detected on the cell surface (i.e., must inherently possess an extracellular region) by staining with the C398.4A antibody (e.g., Figure 3).

Redoglia et al. do not teach that the C398.4A antibody also specifically binds to the polypeptide of SEQ ID NO:2 (human ICOS).

However, Buonfiglio et al. teach the further characterization of the C398.4A antibody, as well as the mouse H4 polypeptide recognized by the C398.4A antibody (see entire document). Buonfiglio et al. establish that the C398.4A antibody which binds to the mouse H4 polypeptide *also binds to L cells transfected with either the human polypeptide previously identified as ICOS*, or with mouse ICOS (see especially page 3465, last paragraph). Buonfiglio et al. conclude based upon the shared antibody reactivity, functional and biochemical properties that *mouse H4 and mouse ICOS are identical* (see entire document, especially page 3466).

Mages et al. teach the characterization and cloning of mouse ICOS, and compare it to human ICOS (see entire document). Mages et al. teach the nucleotide and amino acid sequence of mouse ICOS, which Buonfiglio identify as identical to H4 (see especially Figure 1). Mouse ICOS/H4 is a polypeptide that
has a partial amino acid sequence of FDPPPF in its extracellular region (e.g., Fig 1B); and
has a partial amino acid sequence of YMFM in its cytoplasmic region (e.g., Fig 1B).
Mages et al. also teach that mouse and human ICOS are polypeptides that are highly homologous, having 71.7% identity and 80.6% similarity at the amino acid level (see Figure 1 and Section 2.1 on page 1041). The human ICOS sequence taught by Mages et al. in Figure 1B is identical to instant SEQ ID NO:2.

Thus the C398.4A monoclonal antibody taught by Redoglia et al. also inherently binds a human-derived polypeptide having the amino acid sequence of SEQ ID NO:2. Since the C398.4A antibody binds the polypeptide expressed on cell surfaces, the C398.4A antibody also inherently binds the extracellular region of the polypeptide of SEQ ID NO:2.

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations, including the limitation that the antibody induces adhesion between mitogen-stimulated lymphoblast cell, would be inherent properties of the C398.4A antibody taught by Redoglia et al., as evidenced by the Buonfiglio et al. and Mages et al. references. In addition, especially given the ambiguity noted supra with respect to instant claims 30 and 31; the C398.4A antibody would also inherently have an effect that is "substantially the same as the effect of" monoclonal antibodies FERM BP-5707 and FERM BP-5708. Finally, the intended use of the pharmaceutical composition comprising the antibody does not carry patentable weight per se, and the claims read on the active or essential ingredient of the composition.

With regard to the issue of priority, it is noted that the earliest date which could possibly be established as an effective US filing date is 2/27/98, based upon provision of a certified copy of a translation of PCT/JP98/00837 showing adequate support for the instant claims. Thus the application of the Redoglia et al. reference (November 1996) under 35 USC 102(b) is unaffected by the instant uncertainty regarding Applicant's priority date.

23. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefore ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

24. Claims 27-34 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 27-34 of copending Application No. 09/561,308. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

25. No claim is allowed.

26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica H. Roark, whose telephone number is (703) 605-1209. The examiner can normally be reached Monday to Friday, 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Jessica Roark, Ph.D.
Patent Examiner
Technology Center 1600
January 16, 2002

PHILLIP GAMBEL, PH.D
PRIMARY EXAMINER
TECH CENTER 1600
1/17/02